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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,274	12/06/2005	Wen-Hwa Lee	21105.0004U2	3628

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,274	LEE ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11-16,21,22,24-31,37-39 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *21,22 and 24-26* is/are allowed.

6)☒ Claim(s) *1,11-16,28,29,37-39,42* is/are rejected.

7)☒ Claim(s) *27,30 and 31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 2-5, 8, 17-20, 23, 32-36, 40 and 41 have been canceled. Claims 1, 21, 22, 24, 25, 27, 28 and 37-39 have been amended. Claims 1, 11-16, 21, 22, 24-31, 37-39 and 42 are pending and under consideration.

Claim 27 is objected to because of the following informalities: the typographical error of "Hin 1" rather than "Hint1". Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 37 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re wands, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988)..

Claim 37 is drawn to a method for treating a disease involving cell hyperproliferation, including cancer and stenosis, comprising the administration of a molecule termed IBT13131 or a molecule termed IBT14664 The specification provided a yeast two-hybrid screen to identify eight molecules that inhibit the interaction between Hec1 and Nek2 (page 40, lines 15-31) in yeast. The specification teaches that out of the eight molecules, IBT13131 and IBT14664, showed the ability to kill dividing HeLa cells (page 41, lines 8-28). The at teaches a number of cellular proteins in addition to nek2 that bind to Hec1, wherein the mutant phenotype of said

proteins caused G2/M phase arrest (Clark et al, WO98/45433, page 46). The art recognizes that many compounds can show favorable activity in vitro but fail to show favorable activity in a clinical treatment. Mohanlal (WO0240717) teaches that an important reason for the high failure rate in clinical trials is the poor predictive value of currently used screening technologies for biological validation, pharmacological testing, and screening for success or failure of chemical entities and biologicals in clinical trials involving human subjects, which include screening based on in vitro assays, which inadequately represent the clinical disease phenotype of the patients in which the tested chemical entities or biologicals are intended to be used in the future. Mohanlal teaches that success of chemical entities or biologicals in cell screens does not necessarily translate into clinical success in patients because the majority of chemical entities or biologicals, while successful in said cell screens fail in clinical trials, particularly in late phase II and phase III trials for pharmacodynamic reasons (lack of efficacy and/or an unacceptable adverse event profile); and pharmacokinetic reasons. In the instant case, the specification teaches only toxicity toward Hela cells and Saos2 cells (page 42, lines 15-19) which provides not information on pharmacodynamics or pharmacokinetics. It is concluded that the potential to treat a subject suffering from a hyperproliferative disease or cancer by the administration of IBT13131 and IBT14664, has not been established by the specification. Thus, one of skill in the art would be subjected to undue experimentation without reasonable expectation of success in order to carry out the method of claim 37.

Applicant has reduced the scope of the claim, but has not provided a persuasive argument regarding the treatment of a subject for cancer or a hyperproliferative disorder by the administration of IBT13131 and IBT14664.

Claims 1, 11-16, 39 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 has been amended to delete reference to the inhibition of the interaction between Hec1 and at least one further protein. Thus, when given the broadest reasonable interpretation,

the claims encompass any method wherein a subject is treated with a compound comprising (4-phenylthiazol-2-yl) benzamide and hyperproliferation or cancer is modulated thereby..

The originally filed disclose describes a method wherein cancer or hyperproliferation is modulated by virtue of antagonization of the binding between the Hec1 protein and Hint1 or Nek2. This fails to provide a basis for the broad method of treating hyperproliferation or cancer comprising administration of the recited core structure without the requirement that the binding between Hec1 and Hint1 or Nek2 is inhibited. One of skill in the art would reasonable conclude that applicant was not in possession of the claimed invention at the time of filing.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 11-16, 38, 39 and 42 are rejected under 35 U.S.C. 102(a) as being anticipated by Koshio et al (WO02/062775), as evidenced by Koshio et al (U.S. 2004/0077697, English Equivalent).

Claim 1 is drawn to a method of treating a disease involving cancer and hyperproliferation comprising the administration of a compound containing a core N-(4-phenylthiazol-2-yl)benzamide structure thereby lessening cell hyperproliferation. Claim 11 embodies the method of claim 1 wherein the disease is a cancer. Claims 12-16 and 42 specify various types of cancers. Claim 39 requires that the core N-(4-phenylthiazol-2-yl)benzamide structure include additional groups on the benzene ring.

Koshio et al (English equivalent) disclose the administration of pharmaceutical compositions of 3,5-dimethoxy-N-(5-morpholin-4-yl-4-phenylthiazol-2-yl)benzamide, N-[5-(4-cyclohexylpiperazin-1-yl)-4-(4-fluorophenyl)thiazol-2-yl]-2-methoxyisonicotinamide, or 3-chloro-N-[5-(4-cyclohexylpiperazin-1-yl)-4-(4-fluorophenyl)thiazol-2yl]-4-hydroxybenzamide

(claim 4) for the administration to a subject to treat thrombocytopenia (paragraphs [0013], [0062], [0068] and [0070]). The disclosure of 3-chloro-N-[5-(4-cyclohexylpiperazin-1-yl)-4-(4-fluorophenyl)thiazol-2yl]-4-hydroxybenzamide meets the requirement of claim 39 requiring an additional group on the benzene ring.

It is noted that the phrase "thereby lessening cell hyperproliferation" is not given patentable weight when comparing the claims to the prior art as it simply expresses the intended result of a process step positively recited, see MPEP 2111.04.

Given that the method of the prior art comprises the same method steps as claimed in the instant invention, the administration of a compound comprising a core N-(4-phenylthiazol-2-yl)benzamide structure, the claimed method is anticipated because the method will inherently be a method for treating cell hyperproliferation and various cancers. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Claim 38 is a product-by-process claim.

Section 2113 of the MPEP states:

PRODUCT-BY-PROCESS CLAIMS ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

.

In the instant case, the compounds of Koshio et al meet the structural limitations of a core N-(4-phenylthiazol-2-yl)benzamide structure and therefore anticipate claim 38.

Claims 1, 11-16 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Kinoshita et al (U.S. 5,112,867).

Kinoshita et al disclose a method comprising the administration of a pharmaceutical composition comprising 2-[Bis(4-hydroxyphenyl)methyl]-N-(4-phenylthiazol-2-yl)benzamide to a subject (column 14, lines 65-68, column 40, lines 47-55 and column 43, Example 18) for the treatment of osteoporosis (abstract).

It is noted that the phrase "thereby lessening cell hyperproliferation" is not given patentable weight when comparing the claims to the prior art as it simply expresses the intended result of a process step positively recited, see MPEP 2111.04.

Given that the method of the prior art comprises the same method steps as claimed in the instant invention, the administration of a compound comprising a core N-(4-phenylthiazol-2-yl)benzamide structure, the claimed method is anticipated because the method will inherently be a method for treating cell hyperproliferation and various cancers. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

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.

In the instant case, the compound of Kinoshita et al meet the structural limitations of a core N-(4-phenylthiazol-2-yl)benzamide structure and therefore anticipate claim 38.

The rejection of claims 28 and 29 under 35 U.S.C. 102(b) as being anticipated by Clark et al (WO98/45433) is maintained for reasons of record.

Claim 28 is drawn in part to a method comprising the steps of contacting a sample comprising cells with a molecule or a combination of molecules and measuring the amount of cell cycle proliferation and arrest. Claim 29 embodies the method of claim 28 wherein the sample comprises isolated cells

Clark et al disclose a method comprising the steps of making an anti-Hec1 antibody which fulfills the requirements of "designing a ligand" and "designed from a known compound" of claims 32 and 35. Clark et al disclose that injection of the anti-Hec1 antibody into cells does not arrest cells in mitosis but allows said cells to proceed aberrantly (page 15,, lines 16-18),

Clark et al disclose a method wherein transfection of cells with a Hec mutant protein containing only the long series of leonine heptad repeats and to interact through said repeats with several protein important for mitosis including Nek2 (page 4, lines 17-22).. Clark et al disclose that the in vivo binding of the mutant Hec protein and the interacting proteins was determining by reciprocal co-immunoprecipitations (page 46, Table 3) which fulfills the limitations of claims. Clark et al disclose that the transfection of the dominant negative Hec1 protein caused G2/M arrest (page 46, Table 3) which meets the specific embodiment of claims 28 and 29 with regard. to cell cycle progression and arrest. Further, Clark et al disclose a method of disordering sister chromatid alignment, comprising administering to an interphase cell an amount of an antibody that specifically binds to HEC, wherein mitosis is disrupted (claim 18). The disruption of mitosis meets the specific limitations of interfering with the cell cycle, and the binding of the anti-Hec antibody to Hec interferes with the function of Hec thus the limitation of claims 28 and 29.

Applicant states that the limitation of determining the interaction between Hec 1 and Hint1 is now part of claim 21. This has been considered but found only persuasive to claim 21, and claims dependent therefrom. Claim 28 does not require the measurement of interference between Hec 1 and Hint1, because Hec1, Nek2 and Hint1 are listed in alternative form, and the function of only one protein need be determined.

Claims 21, 22, 24-26 are allowable.

Claim 27 is objected to for a typographical error.

Claims 30 and 31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643